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Patentanmeldung Nr. Patent application No. Demande de brevet n°

99200166.9

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Der Präsident des Europäischen Patentamts:
Im Auftrag

For the President of the European Patent Office

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Page 2 de l'attestation

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Applicant(s):
Demandeur(s):
N.V. Nutricia
2700 MA Zoetermeer
NETHERLANDS

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Infant formula

Field of the invention

[1] The invention is related to infant formulae, i.e. artificial product for complete nutrition of infants, for improving feelings of well-being, compensation of immaturity and problems in the metabolic capacity of the infant. The nutritional products provide complete nutrition to the infant and her composition is characterised by the selected protein and carbohydrate composition and the increased amounts of folic acid, and vitamin B6 and B12 or their functional analogues.

Background of the invention

[2] At present a large part of the population of babies in industrialised countries are fed with specialised infant formulae. It has been reported that consumption of these formulae is associated with several medical problems that may occur at young age, such as increased frequency of gastrointestinal problems and decreased immune status, but perhaps also at later age, because infants that are exclusively fed with human breast milk would score better on these parameters. It has also been reported that infants that are exclusively fed with these artificial formulae suffer from longer episodes of crying compared to those that are fed with human breast milk. This suggests a general feeling of discomfort due to perhaps hunger, pain or even medical problems. These problems may delay development of the child and produce concerns and practical problems to the parents.

[3] In a first aspect of the invention it is aimed to develop a new infant formula for complete nutrition that decreases the number of crying episodes for the child, especially for infants of young gestational age.

[4] In a second aspect it is also aimed to develop infant formulae that compensate for the relatively small capacity of the (rapidly developing) metabolic systems of the child shortly after birth. This leads to improved health, formation of higher quality new tissue (visual acuity, intellectual capacities, etc.), a better immune status and a decrease in occurrence of periods of increased bilirubin plasma levels (hyperbilirubinaemia or jaundice). Increased bilirubin levels are known to occur relatively often within the first 3 weeks after birth. Some of the negative effects of this disorder have been described properly in the prior art, including the inhibition by bilirubin of the uptake of the neurotransmitters dopamine and glutamate by the synaptic vesicles and the neurotoxic effects that this disease state may have.

[5] Conventional infant formulae have been developed that mimic the composition of

human breast milk to a degree that can be achieved at a reasonable price. These formulae are normally based on cow's milk proteins like casein or mixtures of casein and whey. In case of problems, such as metabolic disorders or allergic reactions, other protein sources are used like hydrolysates or soybean proteins; alternatively the allergic component is replaced by another non-allergenic ingredient. However, the composition of these formulae still differs from that of human breast milk. The relatively low levels of tryptophan and cysteine/cystine can be compensated for by increasing the amount of protein in the product. However, this increases the amount of threonine to very high levels and increases the costs of the formulae. Also the imbalances with regard to the ratio of tryptophan to the sum of the large neutral amino acids will be maintained.

[6] In a third aspect of the invention, it is therefore aimed to develop a formula that provides amounts of tryptophan, cysteine and threonine that are more similar to when exclusively human breast milk is consumed, while at the same time the value of the ratio of the amounts of tryptophan to large neutral amino acids in the product, is more similar to the value is observed in human breast milk. Plasma levels of the amino acids in infants that are exclusively fed with the new composition will therefore be more similar to those observed in infants that are exclusively fed with human breast milk. At the same time the costs and taste of the nutritional product will be acceptable.

[7] Serotonin (5-hydroxytryptamine) is an important neurotransmitter, especially in the central nervous system. It also behaves as a strong contractor of smooth muscles, for example those in the arterioles and bronchioles, when released from mast cells and platelets. Serotonin is claimed to be involved in the release of peptic hormones in the gastrointestinal tract. Abnormalities in serotonin metabolism have been linked to several disorders of the central nervous system such as those related to pain, sleep and mood, either by direct action of serotonin or via its role as precursor for melatonin. Serotonin is synthesised from tryptophan by hydroxylation and subsequent decarboxylation. Tryptophan has to pass the blood brain barrier first, before it can be converted in the brain to serotonin. This passage occurs via a receptor that also transfers the large neutral amino acids.

[8] "Large neutral amino acids" are understood to be valine, isoleucine, leucine, tyrosine and phenylalanine. In order to obtain relatively high amounts of tryptophan in the brain, competition by these amino acids has to be low and consequently the ratio of plasma concentrations of tryptophan and the sum of the large neutral amino acids has to be large.

[9] It has been found that threonine also uses this same receptor. It is now recognised that because of the high amounts of threonine in conventional cow's milk sweet whey, that high threonine plasma levels are obtained that the passage of tryptophan over the blood brain

barrier is significantly hindered. In a fourth aspect of the invention it is therefore aimed to provide an infant formula that ensures an increased ratio of the plasma concentrations of tryptophan to the sum of the large neutral amino acids plus threonine.

[10] After consumption of carbohydrates, insulin is released from the pancreas. This latter component is known to turn the catabolic processes in the body, that may have resulted from a period of starvation prior to the (re)feeding of the child, into anabolic processes. As long as sufficient glucose is present in the plasma, plasma insulin levels remain sufficiently high to prevent catabolism of (in particular muscle) tissue and the resulting release of branched chain amino acids (BCAA, valine, isoleucine and leucine). In a fifth aspect of the invention it is therefore aimed to develop an infant formula that provides an insulin response on a short term.

[11] It is now recognised that the insulin response must also last at least until the next feeding of the infant.Young infants are fed every 2–8 hours. It is equally important that infants maintain appetite and will eat every time a sufficient amount of food in a short time, to ensure sufficient growth. In a sixth aspect of the invention it is therefore aimed to develop a formula that, after consumption, maintains appetite of the infant after 3 hours and at the same time satisfies the infants during a period of at least 1–6 hours and preferably for a period up to 3 hours.

[12] Infants, especially those of young gestational age, are extremely sensitive to consumption of excess amounts of food components and imbalances in the consumption pattern of these components, predominantly due to their low metabolic – and clearance capacity. This is caused by inherited problems and immaturity of their enzymatic systems and the small capacity of their organs. Infants are also sensitive to imbalances in neurotransmitter levels in the brain. It is therefore dangerous to transfer concepts that are developed for adults to infant formulae.The composition of human breast milk is therefore mostly taken as "golden standard". In a seventh aspect of the invention a nutritional product is aimed at that does not cause any toxic reactions in normal use and to deviate as little from the golden standard as is justified.

[13] It is important to recognise that all the aspects as mentioned above must be achieved at the same time, in order to regulate serotonin biosynthesis and metabolism satisfactorily without causing negative effects to the child.

[14] The biochemical roles of folic acid, vitamin B6 and B12 are described in the art. To the best of the knowledge of the inventors, it is nowhere described or indicated that consumption of the combination of these vitamins, in amounts as given in the claims, is crucial for increasing well–being and normalising behaviour, senses of pain, and mood of

the infant. It was found that the restrictions in protein and carbohydrates composition, that are present for infant formulae, necessitate the increase in these vitamins in order to have an optimal effect. It is also not earlier disclosed that inclusion of these vitamins in the amounts as claimed, significantly enlarges the group of infants that benefit from such infant formulae, especially with regard to increase of well-being, the improvement of other serotoninergic or melatonin-mediated disorders.

[15] In Table 1 the composition of a typical formula for infants younger than 4 months is compared with that of human breast milk and that of a formula according the invention. For the purpose of comparing these formulae with compositions as described in the prior art, it is useful to relate the composition to the amount of components that will be consumed per kg body weight per day.

[16] **Table 1: Comparison of the composition of Nutrilon Premium, human breast milk and a composition according to the invention.**

Component	IMF*	HBM**	Invention
Energy (kcal/100ml)	67–70	65	63–71
Crude Protein (g/100ml)	1.3–1.5	0.7–0.8 #	0.7–1.4 #
Arg (%=g/100g protein)	3.0–3.5	4.9	3.4–5.0
Trp (%)	1.3–1.5	3.0	1.6–3.5
BCAA (g/100g protein)	22–25	25.5	19–25
Tyr + Phe	7–9	12.4	7–11
Thr	5–7??	6.0	3–6
Cys	1.0–1.6	1.9	1.5–3.6
Carbohydrates=CHO (g/100ml)	4–7.5	7	5.7–10.5
Lactose (%=g/100g CHO)		80–100	990–100
Maltodextrins (%)	0–20	0	0–100
Folic acid (μg/100 kcal)			30–200
Vitamin B6 (μg/100 kcal)			50–130
Vitamin B12 (μg/100 kcal)			0.1–20
Zinc (mg/100 kcal)			0.4–1
Vitamin B2 (μg/100kcal)			80 –300
Niacin (mg niacin equivalents/100 kcal)			0.55–2.0

Notes: * As an example of a typical IMF (= infant milk formula) was taken a formulae based on 40–60% whey and 40–60% casein
** Average values for mature human breast milk
# these protein levels are specified as real protein which is defined to be the amount of protein + amino acids and peptides.

[17] Conventional infant formulae provide about 63–71 kcal/100 ml. This value is recommended in order to provide 100–130 kcal/kg bw.d, which is generally assumed to be mandatory for adequate growth by the child. Typical protein levels in commercially available infant formulae are 1.2–1.6 g/100ml. This leads to consumption of 2.0–2.4 g protein/kgbw.d. Typical tryptophan levels in the proteins as used in the manufacturing of infant formulae are 1.3–1.5%. This results in typical intakes of 26–36 mg tryptophan/kgbw.d by infants. In infant formulae, whose protein composition is formed by mixing 60% sweet whey and 40% casein, the value of the ratio of the amounts of tryptophan to the total amount of large neutral amino acids (Phe, Tyr, Val, Ile, Leu) is about 4.7. When threonine is considered as large neutral amino acid the value of the ratio becomes 3.9. These values become smaller when more casein is used in the product.

[18] Table 1 does not provide data for all food components. Some components are less important for the invention and are therefore not explicitly specified. However, the product according to the invention require inclusion of these components in amounts as present in conventional infant formula, except in those situations as indicated in the text.

[19] Conventional infant formulae do not support optimally well-being of the child, because the tryptophan levels are much too low, especially compared to the sum of the amounts of large neutral amino acids plus threonine, and because the amounts of all three essential vitamins, being folic acid, vitamin B6 and B12 are insufficient to support biosynthesis and metabolism in the young child.

[20] Kreitzman disclosed in WO 87/01590 (= EP–A–238533) a slimming diet for adults that provides per day less than 1000 kcal (so less than 14 kcal/kgbw.d; less than 700 kcal/day is preferred), less than 100 g protein (which results in <1.4 g protein/kgbw per day for a 70 kg person; always more than 30 g and less than 46 g protein is preferred) and more than 0.5 g tryptophan (more than 3 g is preferred). The product is unsuitable for feeding infants due to too high protein levels and potential toxicity of the amount of tryptophan that is included. The product should also not be used for combatting obesity of the infant.

[21] EP–A–007691 (Wurtman) discloses a formula for suppression of appetite for carbohydrates in adults, that comprises tryptophan, in an amount of 10–100 mg/kgbw.d, no branched chain amino acids and carbohydrates. The ratio of the amounts of tryptophan and carbohydrates in the formula must be 1 : 3–50. The product is unsuitable for use in infants, because infants require branched chain amino acids at young age for growth. In addition the amount of carbohydrates should always be more than 25 times the tryptophan level in a formula.

[22] Medgennix disclosed in WO 91/10441 (= EP–A–463154) compositions that

comprise polypeptides, that contain more than 2.2% tryptophan as well-as arginine or ornithine for providing a "serotinergic effect". The product is developed for combatting obesity in adults and treating feelings of depression. No reference is made to infant formulae. Preferably α-lactalbumin is used as a source of tryptophan, which possesses a high ratio of tryptophan to large neutral amino acids plus methionine. Vegetable proteins are suggested as attractive ingredients, because of their relatively high amount of arginine and relatively low levels of phenylalanine and tyrosine. The latter two amino acids are however essential amino acids and recommended daily intakes should be ensured.

[23] Laboratoire Oenobial discloses in WO 98/14204 the use of α-lactabumin as nutritional complement or medicine for regulating sleep, especially when a jet lag is observed. Consumption of 100 mg and 250 mg α-lactalbumin is claimed to be effective in adults. No relation is made to use in infants nor is indicated that vitamins might play a role in regulating sleep. Alpha-lactalbumin was shown to have a value of the ratio of tryptophan to the sum of the large neutral amino acids is about 0,074 and that of the ratio Cys to Trp equals about 1.47, while the amount of tryptophan is relatively high (about 3.0%).

[24] Heine disclosed the use of hydrolysed α-lactalbumin as protein source in infant formulae in DE-A-4130284. Use of this protein hydrolysate was claimed in order to achieve a clear separation with β-lactoglobulin and thus administer a better balanced composition with regard to threonine, tryptophan and cysteine/cystine. No reference was made to specific positive effects that can be obtained by using intact α-lactalbumin with regard to feelings of well-being nor the support of insufficiently functioning metabolic systems by using the products of the invention. Neither was indicated that folic acid, vitamin B12 and B6 play a crucial role in these respects. The products as disclosed by Heine are also more expensive and have a worse taste compared to the products of our invention.

Detailed description of the invention

[25] The characteristics of the composition according to the invention are described in the claims and Table 1 and in more detail below.

[26] Energy density: The energy density of the product is similar to that of prior art products and is in the range of 62-73 kcal/100ml liquid or reconstituted product. Preferably the energy density is in the range of 64-71 kcal/ml.

[27] Proteins: Protein levels in a product can be determined with the classical Kjeldahl method. The result reflects the crude proteins that are present. For the purpose of this invention we define the protein level as the amount of real proteins plus the amount of amino acids, their salts and peptides; so non-protein nitrogen is excluded. In the products

of the invention the protein levels will be in the range of 1.0–2.4 g/100 kcal, which allows complete satisfaction of the infants protein needs. An amount of 1.5–2.2 g/100 kcal is preferred. As protein source conventional proteins like those from cow's milk or soybeans can be used as bases, because they provide sufficient amounts of all essential amino acids but also branched chain amino acids.

[28] In order to increase the amount of L–tryptophan in the product, free L–tryptophan, or functional equivalents thereof like tryptophan salts or tryptophan–rich peptides, can be suppleted. If free L–tryptophan is used, special care is taken to remove all impurities that might cause toxic reactions. It is further preferred to use a tryptophan source that is stable under the conditions that the infant formula is manufactured. A suitable source is a tryptophan–rich protein or a hydrolysate or extract thereof. If proteins are used as ingredient, it is obvious that the levels of the large neutral amino acids and threonine are relatively low. However they should not be that low, that the recommended daily intakes are not met. Examples of suitable proteins in this respect are acid whey, α–lactalbumin, egg protein and proteins from meat and wheat. Acid whey protein or unhydrolysed α–lactalbumin are especially preferred, because of the excellent amino acid profile and the delayed action in time compared to hydrolysates thereof or compared to a combination of mixtures of alternative dairy products and suppleted sources of tryptophan, cysteine or arginine. Tryptophan should be present in the product in an amount of 1.6–3.5 g per 100 g of the total protein component and preferably in an amount of 1.9–2.8 g/100 g protein.

[29] The value of the ratio of the amounts in the product of tryptophan and the sum of the large neutral amino acids must be in the range 4.8–10 and preferably in the range 5.5–8.5.

[30] When threonine is also considered as a large neutral amino acid, the value of the ratio must be in the range 4.1–8.0 and preferably in the range 4.7–7.5.

[31] In order to ensure sufficiently high levels of cysteine, whey proteins or egg proteins can be included in the formula. If whey proteins are used, acid whey is recommended, in order to avoid too high threonine levels.

[32] It is especially preferred to have a relatively high ratio of Cys/Trp in the range of 0.8–1.4, in order to support optimally inclusion of cysteine in liver proteins and in glutathione, which is required for optimal growth and immune function.

[33] In order to increase insulin response arginine or lysine can be supplied as L–forms of the free amino acid or as their functional equivalents. Functional equivalents of amino acids can for example be their salts, synthetic peptides, or proteins that are rich in that particular amino acid, or extracts or hydrolysates of these proteins. Also mixtures of proteins

can be included. For example mixtures of 40% casein and 60% whey could be suppleted with the hydrochloric salts of L-tryptophan or L-arginine. It is however preferred to include arginine in a form that is slowly released such as by using a granulate or similar system that comprises an arginine salt like L-arginine.HCl, or by using partially pea protein, or a hydrolysate or extract thereof, in order to extent the insulin effect. The total amount of arginine plus lysine should exceed 50 mg per day. The amount of protein that is required for providing this amount of arginine can be calculated from this number and the concentration of arginine or lysine in this protein.

[34] Carbohydrates: According to the invention, the amount of carbohydrates in the formula must be in the range of 9–15 g/100kcal (35–60 en%), and preferably in the range of 11–14 g/ 100 kcal. This results in a carbohydrate content of 5.7–10.5 g per 100 ml of liquid or reconstituted product. The value of the ratio of the amounts of carbohydrates to the amount of tryptophan will exceed 20 and preferably 25, and go up to 625, preferably up to 250. The weight ratio of carbohydrates to protein is preferably from 5 to 14, most preferably from 6 to 12.

[35] It is preferred to use, at least partly, maltodextrins, apart from the lactose that may be present in the formula. This will ensure a fast availability of glucose units in plasma and therefore a fast insulin response. However, it is preferred to include at least 50% of the carbohydrates as lactose, except in those cases that the product will be used by lactose intolerant infants. If maltodextrins are used it is advantageous to use maltodextrins having a degree of hydrolysis of 10–15 dextrin equivalents, in order to decrease the sweetness of the product.

[36] Folic acid: Folic acid can occur in nature in many forms. Typically it is suppleted to infant formulae as monoglutamate. Though according to the invention basically all functional equivalents of folic acid can be used, it is preferred to use the monoglutamate form for obtaining best bioavailability. It is essential to include at least 30 μg, and preferably more than 44 μg per 100 kcal. If higher amounts of folic acid are consumed, a larger group of infants will show an improved serotonin- and melatonin metabolism, even if the amounts of tryptophan are relatively low as in conventional infant formulae. This is especially true if the amount of folic acid is above 50 μg per 100 kcal and sufficient vitamin B12 is made available, as is the case when the formula is suppleted with more than 0.6 μg/ 100 kcal, as is indicated below.

[37] Vitamin B12: Vitamin B12 is normally present in infant formula partially as a complex with dairy proteins and predominantly as suppleted cyanocobalamine. Before it is absorbed the complex has to be split in the stomach and the released cobalamine has to bind

to a factor that is released from the stomach. Once absorbed, cyanocobalamine or alternative forms have to be converted to methylcobalamine, before they can be used as cofactor that catalyses the conversion of homocysteine to methionine. Both absorption and conversion of cyano–cobalamine occur ineffectively in a large part of the population young infants. According to the invention it is therefore required to supplete at least 0.1 μg, and preferably more than 0.8 μg vitamin B12 per 100 kcal, preferably as hydroxycobalamine, in order to support serotonin biosynthesis and metabolism effectively.

[38] As an alternative possibility, the endogenous formation of vitamin B12 by the bacteria in the gut is stimulated. This can be achieved by including stimulating compounds in the composition. It has been found that pyrroloquinoline quinone (PQQ) is extremely useful for this purpose, especially when the amount of PQQ exceeds 5 and preferably 10 μg per 100 kcal. Because this also makes the bacterial gut flora resemble more that of infants that are exclusively fed with human breast milk, it is preferred to combine the two ways of vitamin B12 suppletion. This can be done by suppleting per daily dose 1 μg hydroxy–cobalamine and 60 μg PQQ. As an alternative also food grade microorganisms can be added in lyophilised form that are selected for their high capacity to synthesize vitamin B12 analogues.

[39] When indigestible carbohydrates are added to the product or other bifidogenic measures are taken, these are selected in such a way that the biosynthesis capacity of the gut flora is not imparted or even is stimulated.

[40] Vitamin B6: Vitamin B6 is active in the cells as pyridoxal phosphate. However pyridoxine or pyridoxamine are frequently used as source of this vitamin, because of the stability of these compounds. Infants, especially those of young age, have a restricted capacity to convert these compounds to the active form. It has been found that a simple increase in the dose may decrease the intracellular pyridoxal phosphate levels. It is therefore preferred to include in the formula 50–130 μg vitamin B6 per 100 kcal. If higher amounts of vitamin B6 are suppleted it is not recommended to use pyridoxine. Also mixtures of pyridoxamine or pyridoxal can be used.

[41] Zinc: Because zinc is essential for biosynthesis of pyridoxal phosphate, it is mandatory that the amount of zinc is in the range of 0.4–1 mg/100 kcal. Zinc can be included as zinc salt, such as zinc sulphate or as complex with amino acids or other components.

[42] Niacin: Niacin functions in the human body as precursor of NAD and can be synthesized from tryptophan in the adult liver. This predominantly occurs when excess tryptophan is present. Biosynthesis of niacin is supported in the young child by the

characteristic features of the composition as claimed. This permits the availability of sufficient niacin to support the metabolic processes in the child. These can be further supported by increase of the included amount of niacin to a level of 1.2–2.4 mg/100 kcal.

[43] Apart from the essential components as indicated above, other microingredients should be included in a complete infant formula:

Per 100 kcal should be added: Betaine 2–100 mg, Choline about 7–30 mg; Taurine 2–20 mg; inositol 4–40 mg; Calcium 50–140 mg; phosphorus 20–70 mg; magnesium 4–17 mg; iron 0.2–1.65 mg; manganese 1–100 mg; copper 60–160 µg; iodine 8–35 µg; sodium 25–50 mg; potassium 60–160 mg; chloride 50–160 mg; selenium 1.5–5.0 µg; fluoride 0–60 µg; carnitine 1.2–2.0 mg; nucleotides 0–16 mg; cholesterol 2–100 mg; vit A 200–500 IU; vit D 40–100 IU; vit E 0.5–5 mg α–tocopherol equivalent per gram polyunsaturated fatty acid; vit K 1.0–25 µg; thiamine 30–200 µg; riboflavin 80–300 µg; pantothenic acid 0.3–1.2 mg; biotin 1–15 µg and ascorbic acid 6–15 mg.

[44] Fats are included in the range 40–57 en%. The composition of the fat can be selected from prior art compositions. Specially preferred are the ones that are disclosed in any of the earlier patents of patentee, e.g. EP–A–404058, EP–A–231904, EP–A–784437 and DE 19644518, which are incorporated by reference. The essential fatty acids that are present must preferably have the cis–configuration. Alpha–linolenic acid (=ALA): 1.75–4.0 % and linoleic acid (LA): 8–35% of total fatty acids; the ratio LA/ALA = 6–16.

[45] The product of the invention can have the form of liquid or a powder, that can be reconstituted with water to produce a ready to feed formulation. It can also have the form of a meal that is used for weaning purposes or similar product evident to a person skilled in the art. The liquid products can be packaged in bottles, cartons and the like. The powdered products can be packaged in vacuumised packs, cans or sachets and other suitable forms that are known to a person skilled in the art.

[46] It has been found that daily consumption of the infant formulae as described in the claims results in the benefits as described below:

* improves feelings of well being by the infants, while supporting regular eating and sleeping patterns
* helps to compensates for insufficient capacity of the metabolic systems, especially in the young infant, like becomes evident in jaundice
* consumption of these formulae results in plasma levels of amino acids that are more similar to those of infants, that are exclusively fed with human breast milk, compared to consumption of conventional formulae
* does not give negative side effects

* therefore improves health and immune status and support growth of high quality
* has an excellent taste and can be produced at acceptable costs

Examples

Example 1

A liquid infant formula having the composition as presented in table 2 was prepared.

Table 2: Composition of liquid infant formula

Values are in mg per 100 ml, except where indicated differently.

Protein (60% sweet whey, 40% casein)	1400
Added Trp	10
Added Arg	10
Lactose	7500
Maltodextrins (10–15 DE)	1600
Fat (EP–231904)	3100
Na	18–25
Potassium	60–100
Cl	40–60
Ca	50–85
P	20–50
Mg	4.5–6
Fe	0.5–0.9
Zn	0.6–1.3
Cu	40–60 µg
Mn	5–20 µg
Se	1.5–2.2 µg
I	5–15 µg
Vitamin A	80–90 RE
β–Carotene	0–40 µg
Vitamin D	1–1.6 µg
Vitamin E	0.8–1.4 mg TE
Vitamin K	4–20 µg
Thiamin	35–45 µg
Riboflavin	110–150 µg
Niacin	0.7–0.8 mg NE
Pantothenate	0.25–0.35
Biotin	1.5–1.7 µg
Ascorbic acid	5–10
Taurine	4–7
Folic acid (added as monoglutamate)	25–32 µg
Vitamin B12 (added as hydroxycobalamine)	0.4–0.7 µg
Vitamin B6 (added as pyridoxine)	50–65 µg

Example 2

A powdered infant formula having the same composition as in table 2 is prepared. After reconstitution with water it produces a ready-to-feed liquid formula.

Example 3

A liquid infant formula having the same composition as in table 2 is prepared, except that:

a) the protein component consists of 50% acid whey, 10% α-lactalbumin and 40% casein, and no tryptophan or arginine is suppleted, and

b) the microingredients pyrroloquinoline quinone (PQQ) is added to a concentration of 10 µg/100 ml, folic acid to a concentration of 40 µg/100 ml and cyanocobalamine in a amount of 0.6 µg/100 ml; the energy density is 70 kcal/ml.

Claims

1. A product for complete nutrition of an infant, comprising real protein in the range of 1.0–2.4 g per 100 kcal, the protein being characterised by:

(a) providing 1.6–3.5 g tryptophan per 100 g protein, and

(b) having a weight ratio of tryptophan to the sum of the large neutral amino acids in the range of 4.8–10 : 100.

2. A product according to claim 1, in which the protein is characterised by:

(a) providing 1.9–2.8 g tryptophan per 100 g protein, and/or

(b) having a weight ratio of tryptophan to the sum of the large neutral amino acids in the range of 5.5–8.5 : 100.

3. A product according to claim 1 or, in which the protein is characterised by a weight ratio of tryptophan to the sum of the large neutral amino acids times plus threonine in the range of 4.1–8.0 : 100, preferably in the range of 4.7–7.5 : 100.

4. A product according to any one of claims 1–3, in which the protein has a weight ratio of cysteine plus cystine to tryptophan in the range of 0.8–1.4.

5. A product according to any one of claims 1–4, the product being characterised by providing per 100 kcal one or preferably more of the following:

more than 30 μg folic acid,

more than 50 μg vitamin B6, and/or

more than 0.1 μg vitamin B12

or the functional analogues of these vitamins.

6. A product according to any one of the preceding claims, comprising 8–14 g of carbohydrates per 100 kcal and having a weight ratio of the amount of carbohydrates to tryptophan above 25 up to 625.

7. A product according to any one of the preceding claims, in which tryptophan and/or cysteine are present in polypeptide form.

8. A product according to claim 7, in which unhydrolysed α-lactalbumin or acid whey is used as polypeptide.

9. A product for complete nutrition of an infant, characterised in providing per 100 kcal:

(a) more than 44 μg folic acid, and

(b) more than 0.8 μg vitamin B12

10. A product according to any one of the preceding claims, in which hydroxy cobalamin is used as a source of vitamin B12 and pyridoxal or pyridoxamine as a source of vitamin B6.

11. A product according to any one of the preceding claims, which contains at least 5 and preferably more than 10 μg PQQ per 100 kcal.

12. A product according to any one of the preceding claims, which contains at least 5 mg and preferably more than 30 mg betaine, and/or at least 5 mg taurine per 100 kcal.

13. Use of folic acid, vitamin B6 and B12 in the manufacture of infant formulae, to be used for improving senses of well-being, control of feeling of pain and improvement of mood, or treatment or prevention of other serotonin – or melatonin–mediated disorders.

Abstract

The invention relates to products for complete nutrition of infants. The products are characterised by the type and amount of protein and carbohydrate and the increased levels of folic acid, vitamin B6 and vitamin B12 or their functional equivalents. These products improve feelings of well-being of infants, especially those of young age, and are useful in the treatment and prevention of diseases that are associated with disorders of serotonin – and melatonin metabolism.